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Original Communications.

THE CHEMICAL RELATIONS OF BACTERIA.

(A Review of our knowledge of the subject, with some applications to the solution of problems in practical medicine.)

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THE influence of microörganisms in chemical processes remained unrecognized by the earliest investigators. Arabian alchemists and Aristotelian philosophers, apparently, never gave the subject thought. Valentine, in his search for the elixir vitæ, and Paracelsus, in his medico-chemical speculations, were never haunted by microbic visions. In fact microscopy was a very feeble aid in scientific investigation, even at the time when Leeuwenhoek (in 1680) discovered the yeast globules. The germs of chemical discoveries, like those of microörganisms, often remain dried and withered, now free-floating, at another time stationary, and are aroused to suitable growth when the conditions are favorable. From 1680 to 1835 is a long stretch; yet 1835 was the year in which Schwann and Cagniard De Latour watched the budding of the yeast cells. The employment of the historical method in the discussion of biological progress, from the days of Carnèature to those of Pasteur and Koch, would introduce us to the labors of such eminent men of science as Ampere, Turpin, Liebig, Tyndall, and Lister.

When we direct our attention to the fermentation of beer and other alcoholic preparations, to the formation of vinegar, to secale cornutum as the work of the pyrenomycete, ergot, we are convinced that micro-fungi are not to be undervalued in a chemical way. Interesting as these and many allied processes are, they have already been treated of at length in various text-books and monographs, and their discussion, moreover, would transcend the limits of this paper, which is restricted to a consideration of the mutual relations of chemistry and bacteriology. The last-mentioned field is comparatively recent, and as its development is in its infancy, we can but faintly outline its great potentialities.

That there are important relations between chemistry and bacterial investigation will not be denied by one familiar with the processes and results to which I have previously referred. Nor will such relations be considered impossible by one conversant with the *interdependence of all the sciences*. Witness the dependence of geology upon chemistry, physics, astronomy, and other sciences.

We are prone to pay more attention to the violent, irregular manifestations of natural forces than we do to the continued operation of less striking and apparently minuter agencies. Catastrophism prevailed in the infancy of the science of geology. The slow operation, however, of almost invisible forces has produced results which exceed in importance the violent efforts of catastrophism. In geological history the ripple has left a mark which endures as well as the effect of some huge wave. In the presence of volcanic activity we stand with awe, and are apt to be unmindful of the agency of the earthworm in modifying the earth's crust.

That fungi produce chemical changes and decompositions, that the products of their activity are often deleterious poisons, are not unfamiliar facts. Wall-papers, colored by Schweinfurt green or other arsenical pigments, when pasted on damp walls are liable to give off arseniuretted hydrogen, a deadly gas (Wagner, *Chemical Technology*, p. 58, Crookes' edition). In order to explain the evil effects of such arsenical wall-papers Roscoe and Schorlemmer say (*Manual of Chemistry*, Vol. I, p. 520):

"Hydrogen is evolved during the growth of mould and of certain fungi, and it is possible that, if arsenic compounds are present where such growths are going on, arseniuretted hydrogen may be evolved." (In justice to the authors it must be said that other causes are also given by them.) One familiar with fermentation and putrefaction would not doubt the influence of bacterial life in the chemical processes of the earth and the life of its inhabitants.

The subject naturally divides itself into two parts: First, we have to consider the relations of bacteria to chemistry, either as contributing to the formation of chemical products or as a factor in the processes of analytical chemistry. Into the second portion falls the enumeration of the applications of chemistry to the culture and biological analysis of bacteria.

I. *Relations of Bacteria to Chemistry.*—A. *Chemical Products of Bacteria.* According to Parkes, Erdmann (in *Journal für Prakt. Chem.*, XCIX, p. 385) discovered that vibriones have the power of producing aniline coloring matters from protein substances. Bacteria which form pigments of various shades are classed as pigment or chromogene bacteria. Ziegler says that coloring matters are produced by bacteria, which may be "red, yellow, green, blue, and violet." A peculiar growth on the surface of bread was long attributed to miraculous agencies. This growth covered bread with a film as red as blood, and many, therefore, called the bread "bleeding bread." We

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now understand that this phenomenon is the work of micrococcus prodigiosus. If boiled eggs are exposed to a damp atmosphere we sometimes find their surfaces tinged yellow from the work of an organism called micrococcus luteus. The surgeon often finds the bandages which envelop a pus-producing surface stained blue, and this he is now taught to refer to the development of a specific organism (micrococcus cyaneus) in the wound discharges. This phenomenon has been called cyanochrosis, and is due to the development of pyocyanine, a crystalline chemical body (unconnected with the coloring matters of the body, but solely due to the work of microorganism upon the albuminous substances in the wound discharges). Pyocyanine may decompose and form a *yellow* substance (pyoxanthose). The proportions of these two coloring matters influence the color of the pus. (*Holmes' System of Surgery*, Amer. ed., Lea, Vol. I, p. 336.) The list of chromogene bacteria is being extended rapidly. Trelease, in a paper on "Several Zoöglœæ and Related Forms," describes several new species, viz.: Bacterium Candidum, B. Luteum, B. Aurantiacum, B. Chlorinum, and B. Incarnatum. In the *American Association of Science* number for 1885 we find the following extract: "Drs. D. E. Salmon and T. Smith, of Washington, D. C., read a paper on a new chromogenous bacillus [Bacillus Luteus Suis.] This form is non-pathogenic, and was found in the pericardial and peritoneal fluids in swine killed for the purpose of studying the swine fever. When grown in a meat infusion the liquid becomes pale straw color, then orange with a greenish tint, soon changing to a wine red. The pigment when obtained pure is insoluble in alcohol or ether. An aqueous solution is decolorized by adding an excess of strong H NO_3 or HCl, but reappears on neutralizing with potassium hydrate or ammonia."

In some forms of fermentation the production of chemical compounds, as a resultant of the growth of ferment bacteria in lifeless organic materials, is exemplified by a large number of formed substances. Complex organic molecules are split up into simpler forms. As is well known when bacteria are grown in a suitable medium, they withdraw from that medium some inorganic salts, as well as carbon, hydrogen, oxygen, or nitrogen, and at the same time there are to be found in the media certain very interesting products. Without attempting here to enter into a discussion of the ultimate cause of these phenomena (*i. e.*, whether or not due to the direct vegetative action of bacteria), we propose to give a few examples of the formed products.

Milk is rendered sour by bacteria, and here we have the change of milk sugar into lactic acid, the lactic acid fermentation. The formation of rancid butter furnishes us an example of another bacterial fermentative process, the butyric acid fermentation. It has long been observed that we have in certain wines a slimy precipitate, which is supposed to result from the transformation, by bacteria, of the sugar of the wines into a gummy substance. Prof. W. McMurtrie, in a paper read before the Buffalo (1886) meeting of the American Association for the Advancement of Science, contends that "blue milk and ropy cream" are not due to a *simple* chemical change but are the work of some form of bacteria. Prof. Burrill has said (*Botan. Gazette*, Vol. XI, p. 224), "While he did not doubt that it was due to germs, yet he had been unable to decide upon the particular kind."

Some observers have declared that bread fermentation is not due to Engel's saccharomyces, but is the result of a "bacterium found in the leaven." According to Laurent there is a bacillus whose germs exist on the surface of grains of wheat and other cereals, which, by grinding, is mixed with the flour. When this *bacillus panificans* develops in dough it gives rise to carbonic acid which "causes the bread to rise." This organized ferment renders gluten insoluble, and sometimes transforms the starch into Erythrodextrin. It is stated that this microörganism may be detected in the fæces of bread-eaters. This subject has been lately brought to our notice in this country by Dr. E. V. Stoddard in Therapeutic Notes in *Medical Press* of Western New York, July, '86.

Dr. Knapp (*Medical News*, Vol. XLIX, p. 716) defines putrefaction as the "splitting up of a nitrogenous substance through the agency of microbes." Putrefaction is microbic decomposition of dead nitrogenous substances. Suppuration is a similar chemical change, as the result of microbic agency upon living nitrogenous bodies. The subject of chemical changes in putrefaction and suppuration is of the greatest practical import to the physician. Says Dr. Hauser (*Über Fäulniss-Bacterien und Deren Beziehungen zur Septicämie*, Leipzig, 1885): "Panum first pointed out that in the putrefaction of albuminous bodies there was formed a substance of eminently poisonous properties, the so-called 'putrid poison,' non-volatile and insoluble in water, and Bergman at a later date succeeded in isolating this substance in the form of a crystalline body, the sulphate of sepsin. A long series of chemical investigations by other authors followed these researches, in which a large number of more or less poisonous substances, the so-called ptomaines, were recognized as putrefactive products." The results of Dr. Knapp's experiments (*loc. cit.*) "went to show that chemical agents do not of themselves produce suppuration."

In addition to the ptomaines we have, according to the results of numerous investigators, an extended series of putrefactive chemical compounds, some of which are of a very complex nature. As an illustration the following list has been compiled (mostly from Ziegler)—a list which is not intended to be complete, but to contain a few noteworthy compounds of microbic origin. Thus we may have the following compounds from putrefaction (see list, p. 363).

One of the principal products of the putrefaction of albuminoids is leucin (amido caproic acid), $C_6H_{13}(NO)_2$. In fact this substance was first detected in putrid cheese. It may also be a product in the putrefactive change in shavings of horn, glue, etc. It is present, in health, in the animal economy, and may be found in various glands (viz., pancreas or liver), and in the pancreatic digestion of proteids.

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Tyrosin $C_9H_{11}(NO)_3$ is often associated with leucin in similar putrefactive changes.

The inorganic compounds, water, carbon dioxide, ammonia, and hydric sulphide are perhaps more generally known as results of putrefaction.

Amines.	Organic Acids.	Nitrogenous Bases.
Methylamine.	Formic Acid	
	Acetic "	Leucin.
Ethylamine.	Propionic "	
	Butyric "	Tyrosin.
Propylamine.	Valerianic "	
	Palmitic "	
	Stearic "	
	Lactic "	
	Succinic "	

Aromatic Bodies.	Unclassified.	Inorganic.
Indol.	Sepsin.	
Phenol.		H_2S.
Cressol.	Ptomaines.	
Pyrocatechin.		H_3N.
Hydroquinone.	Ferments.	
Hydroparacumi-nic Acid.	Toxic Alkaloids.	CO_2.
Paroxyphenyl—Acetic Acid.		

The various substances which have been enumerated are not formed by the same mode of chemical action. Some are the result of the abstraction of oxygen and may be classed as *reduction* products. Others are the results of the assumption of oxygen, and are *oxidation* products. Lastly, some contain H and O (in the proportion of water: H_2O), and may be termed hydration products. Others, again, are termed products of *substitution*.

As previously mentioned the list given above is not complete. This is necessarily so, since the subject is not thoroughly worked up. More extended investigation in a much neglected branch of chemistry, viz., physiological chemistry, may be confidently expected to add much to our knowledge in this direction.

As illustrative of the formation of alkaloids by bacteria, and of the far-reaching importance of their detection and study, we have but to return to a report of the session of August 24th, 1885, of the Academy of Sciences at Paris (as given in *Nature* of September 3d, 1885). Here we find that Pouchet has been investigating the chemical changes which took place in a liquid in which the comma bacillus of Koch had been grown. The report referred to says: "An analysis of this liquid revealed traces of the presence of an alkaloid liquid presenting outward characteristics, such as small and toxic properties, apparently identical with those detected in the dejecta of cholera patients. Should these results be definitely established they would furnish an indirect proof that Koch's microbe is really the pathogenetic agent in cholera."

Vaughn has recently isolated an alkaloid from poisonous cheese which he terms tyrotoxicon. According to Vaughn "the poison is found to be a product of imperfect putrefaction in the cheese." In 1882 Ziegler (*Pathological Anatomy*, Vol. I, William Wood & Co.) pointed out the fact that "highly poisonous substances are formed in many of the bacterial decompositions." He also (*loc. cit.*) says "cadaveric poison, the poison of decaying fish, *cheese*, mussels, etc., are, very probably, the chemical products of special forms of putrefaction." Ice-cream and milk may be rendered poisonous by tyrotoxicon. Dr. Vaughn presented a paper before the Buffalo (1886) session of A. A. A. S. on "Tyrotoxicon (cheese poison): its occurrence in milk," in which he traces the poisonous effects, which sometimes result from milk and ice-cream consumption, to the presence of this ptomaine, which is thought to be due to a microörganism. Dr. Vaughn has also attempted to point out a relationship between cholera infantum and tyrotoxicon (*Medical News*, Vol. XLIX, p. 704).

Certain bitter principles and poisonous alkaloids have been found in fermenting and rotting food, and original work in this direction may throw light upon many cases of food poisoning, and thus be of practical value to physicians. Parkes (*Practical Hygiene*, Vol. I, p. 234, William Wood & Co.) relates a severe case of liver sausage poisoning, which was probably due to the work of minute organisms. In *New Remedies* (for August, 1878, p. 234) may be found an article on the "Cadaver Poison" of the Australian natives, in which it is stated, on the authority of Taplin, that "the inhabitants of the Lower Murray district of Australia are acquainted with the poison of decomposing bodies, and are wont to thrust their spear points into such a body and use the spear, thus armed, as an effective weapon."

Food from vegetable sources as well as from animal quarters may become poisonous through the formation of ptomaines. Dr. L. Forquignon, in the third bulletin of the *Société Mycologique de France*, discusses the "Role of Ptomaines and Leucomaines in Mushroom Poisoning." In reference to the special bacteria which cause putrefaction, we can say that many species have been found which are associated in this process. Cohn considered bacterium termo as the "primary cause of putrefaction, the real saprogenous ferment." Hauser (*loc. cit.*) differs from Cohn, and considers proteus species to be the real putrefactive bacteria. He says (p. 88, *loc. cit.*): "In putrefaction produced by the proteus bacteria no *inorganic* ferment is produced, and putrefactive decomposition of albuminoids produced by them is evidently to be considered a direct work performance of the bacteria themselves;" and, "The proteus species produce, in putrefactive decomposition of animal tissues, a powerful *poison*, of which a small amount suffices, when introduced into the blood or lymph channels, to destroy small animals, with all the appearances of putrid intoxication or septicæmia."

The relation of bacteria to the digestive fluids of the body we will consider under two heads:

1st. The relation of bacteria to the chemical composition of the digestive products.

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As a result of pancreatic digestion we have indol. This substance may be obtained from indigo by a complex chemical process, and is called a reduction product of indigo. Concerning this substance, Foster, in his *Text-Book on Physiology* (Lea's edition, 1880, p. 337), says: "A pancreatic digestive mixture soon becomes swarming with bacteria;" and, "Kühne found no indol produced when pancreatic digestion was carried on in the presence of *salicylic acid, which prevents* the development of bacteria and like organisms."

2d. The action of the digestive fluids upon bacteria.

According to some researches of Dr. Miller, of Austria, an acid reaction of gastric juice will destroy the bacteria of zymotic diseases, but if the same bacteria are "passed into the stomach before the hydrochloric acid of the gastric juice is poured out they pass on into the intestine uninjured" (*Botanical Gazette*, Vol. XI, p. 287). The bearing of these researches of Miller and of Vaughn, upon the etiology of infectious gastro-intestinal diseases, is self-evident.

Bacteria are generally regarded as something to be dreaded, since they are supposed to cause many diseases; as something to be shunned, since they produce corruption and its attendant foul odor. Yet there are ways in which bacteria serve as valuable friends or assistants in all life, whether animal or vegetable in its nature. As has been pointed out bacteria generate (when invading decomposing organic matter) compounds such as water, carbon, dioxide, ammonia, etc. These compounds are eliminated from inert and useless bodies and made to serve again as plant food. Plants need to have soluble food, and it is probable that they indirectly have some power of rendering food soluble. From decaying vegetation we obtain organic acids, such as humic, geic, ulmic, etc. These acids are quite powerful solvents, and in the light of the present the sequence might read: bacteria, decaying vegetation; organic acids, soluble food.

According to Dr. Hüppe (*Die Methoden der Bakterien Forschung*, first edition, p. 160), it was first experimentally detected by Schlösing and Müntz that through the agency of bacteria the ammoniacal compounds, resulting from the decomposition of organic bodies, were changed into nitric acid. Wollny also claimed that microörganisms had the power of transforming, by oxidation, the carbon of the soil into carbonic acid. Gayon and Du Petit also claimed that bacteria could effect a reduction of nitrate in soil layers where the entrance of air was limited. M. Berthelot, in a communication to the Paris Academy of Sciences (October 26th, 1885), presented a paper on the "Direct Fixation of Free Atmospheric Nitrogen in Plants," of which the following synopsis is given: "After fresh experiments conducted for two years at the Meudon Station for vegetable chemistry, he has discovered a new and perhaps a more general cause of this arrestation in the silent but incessant action of orgillaceous clays and of the *microscopic organisms* contained in them. In this memoir he gives the result of over 500 analyses of four different clays, constituting five distinct but simultaneous series of experiments in a closed chamber, in a field under shelter, on top of a tower twenty-eight metres high without shelter, in hermetically sealed flasks, and, lastly, in soil artificially sterilized."

This subject is also ably discussed by Mr. Francis Sutton, F.C.S., in the Sixteenth Annual Report of the Norfolk and Norwich Naturalists' Society, in a paper on "The Nitrification of Soils by means of Minute Living Organisms." The study of the relations of bacteria to what has been termed the "everyday work of the redistributing agencies of nature upon moribund vegetable matter," is thus of the highest agricultural and economic importance. (Consult Wollny—*Ueber die Thaetigigkeit Niederer Organismen im Boden.*) Some experiments of Duclaux seem to prove that plants absolutely need bacterial aid to make use of the stores of organic matter around them. He found that peas and beans would not thrive in a soil thoroughly sterilized, and Pasteur has expressed the opinion that "life is impossible without the coöperation of microbes" (*Science*, Vol. V, No. 113, p. 208). We have been made familiar with the fact that the atmosphere constantly contains bacteria or their germs, but are not as conversant with the fact that *soils* are filled with them to a considerable depth. According to Pumpelly (*Science*, July 10th, 1885) all the finer soils have the power of filtering or restraining the germs of bacteria, yet soils, however fine, have not the power to prevent the passage through them of water laden with bacterial germs. In Pumpelly's and Smith's investigations for the National Board of Health it was found that filtration through a pipe 100 feet long and filled with sterilized sand was insufficient to prevent water containing bacteria, and, filtered through this pipe, filled with the sterilized sand, from causing putrefaction when dropped into a sterilized infusion of beef. If this water still retained bacteria after so long a journey need we wonder when told that bacteria or their germs may penetrate or find their way to considerable depths in the soil? If they did not pass but a few inches into the soil, or into what has been termed the "ante-chamber of life," we could still see room for them to produce great changes. The simple burial of the excreta of typhoid fever or cholera a few inches below the surface is thus insufficient to prevent worms bringing up the specific germs to the upper layers, which are then taken up by air or water and disseminated we know not where.

Concerning the first few inches of the earth's surface Prof. Pumpelly says: "It is the laboratory in which operate incessantly the processes by which inert matter is prepared for the nourishment of life. It is this because it is also the tomb of all terrestrial living matter. Here is the realization of the phœnix myth; the slow combustion of organic matter, leaving a residuum from which springs the new life of succeeding generations."

Bacteria engage in this work, and have been termed "*our best scavengers.*" No better work could be done by them than the transformation of quantities of dead organic matter into some of the simpler gases we have

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mentioned, or into other useful but more complex substances. It is sufficient to imagine what the condition of affairs on the surface of the earth would be without some work of this nature. Invisibly and silently microörganisms perform this necessary work.

B. *Relations of the Bacteria to Chemical Analysis.*—We note, first, that bacteria have been used as chemical tests for the presence of oxygen. Nor is this thought as striking as at first appears. For a long time it has been known that minute microscopic plants (protococcus) give evidence of the presence of phosphates in solutions. Engelmann has given us a simple test for oxygen: by placing a portion of plant tissue which is giving off oxygen, as a result of assimilation, in the neighborhood of *quiescent bacteria*, and placing the apparatus under a microscope, we behold the bacteria executing vigorous movements, which cease when anything (as withdrawal of the source of illumination) interferes with the exhalation of oxygen. Engelmann says (*Science*, Vol. I, p. 332): "By their presence it is possible to detect the one-trillionth of a milligram of oxygen."

Bacteria often deteriorate volumetric test solutions of litmus, and care should be taken to preserve the same uninfected (Classen: *Handbuch der Analytischen Chemie*, part ii, third German edition, p. 330).

In the analysis of water for sanitary investigations it has been claimed that a microscopic examination for bacteria will give us the most reliable method of judging of the wholesomeness of a water. The extreme adherents to this view assert that the ordinary chemical water analysis does not furnish reliable data. Some one has observed that if this be true at present the future work of the chemical analyst will determine the chemical characteristics of a water which contains bacteria. Lex (Parke's *Practical Hygiene*, p. 71, American edition) has shown us that "besides oxygen three conditions must be present: (1) An organic carbonaceous substance; (2) a nitrogenous substance which need not be organic, a *nitrate* will well nourish bacteria and is reduced to nitrite by their growth; (3) a phosphate, which, however, may be in exceeding small quantity."

In *air analysis* apparatus for the detection and estimation of bacteria in the atmosphere will be used to supplement ordinary chemical methods by examination. Tyndale has familiarized us with the employment of a beam of electric light for detection of germs ("Floating Matter in the Air in Relation to Putrefaction and Infection"). Recently several forms of apparatus have been proposed for quantitative use, and we are enabled to determine the quantity of bacteria present in the air at different hours of the day, different seasons, and under various conditions of moisture. This is a great advance over the simple *qualitative* aeroscope first invented.

The announcement of the presence of ptomaines in decomposing animal bodies was coupled with the fear "that the presence of these compounds would endanger the correctness or reliability of toxicological analysis for poisonous alkaloids administered with criminal intent." Although ptomaines may interfere with the application of special tests, yet it seems that the more commonly occurring alkaloids can be readily distinguished by their well-known reactions (*New Remedies*, June, 1882, p. 189).

To sum up, then, the conclusions deduced from the first part of our subject we agree with the statements made by Sir Lyon Playfair in his inaugural address before the British Association for 1885: "These micro-organisms, the latest contributions to our knowledge of air, perform great analytical functions in organic nature, and are the means of converting much of its potential energy into actual energy."

II. *The Applications of Chemical Methods to the Culture and Biological Analysis of Bacteria.* (a) *Culture Media.*—The ways in which chemical methods are applied to the preparation of culture media are numerous and important. It is self-evident that culture methods, which are without objection in the nature or composition of the media, should alone be employed. The chemical composition of media, in which bacteria naturally flourish, is first ascertained, and secondly, the artificial combinations, which best meet the wants of the observer, are determined.

The first experiments of Pasteur and others were made in transparent liquid media, whose composition was similar to the original liquid, in which the bacteria under investigation were found. Investigators soon learned the intimate dependence of bacteria upon their "base of supplies." The composition of Pasteur's liquid was:

Ammonium tartrate	part 1
Sugar	parts 10
Water	parts 100
Yeast ash in small quantities.	

Mayer and Cohn introduced modifications of this liquid. Naegeli, in 1882, put forward the theory that nitrogen "is best assimilated when present, as H_2N, not as well in the form of HN, still less as NO, and not at all when joined to other elements than H or O." Naegeli, on the basis of the above theory (in part at least), proposed several graded scales or tables of the most approved materials, and from these tables constructed formulæ for the preparation of normal liquids for schizomycetes. (A list is given in Hüppe: *Bakterien Forschung*, p. 74.) Koch's use of gelatine and blood serum, in preparing transparent media and the chemical composition of the same, has been detailed at length in works on bacteriology. Chemical aid is also used in the preparation of beef-extract media, agar agar media, etc., as well as in vegetable solutions of hay, roots, etc.

The *chemical reaction* of the nutrient solution is of the greatest importance. As a rule, solutions are rendered *neutral* or alkaline in bacterial work by the addition of carbonate of sodium.

(*b*) *Staining of Bacteria.—Chemical principles* are also involved in the staining of bacteria. The discovery of the aniline compounds has proved to be of great use in bacteriological investigation. The aniline dyes are divided into a *basic* and an *acid* group, according to the *chemical composition* of the dyes. The chemical properties of the dyes must be comprehended before they can be rightly applied. Their solubilities must be investigated, for upon these the

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preservation, preparation, and composition of staining solutions depend. The preservation of microscopical preparations, the removal of excessive staining, the operation of "clearing"—all these profit by a thorough study of the chemical features of the aniline dyes. Chemistry also aids the "preparer" in removing fat or lime from tissues which are to be stained. The chemical properties of hæmatoxylon, carmine, etc., must be understood. The preparation of menstrua, such as the "aniline water" of Ehrlich, toludine media, etc., requires an intelligent application of chemical processes. Since chloroform is a solvent of basic aniline colors Canada balsam, when used to preserve specimens stained with these colors, must be thinned with turpentine or xylol. For similar reasons we cannot use oil of cloves as a clearing medium, but resort to oil of turpentine, cedar, or bergamot. Glycerine is used with only the brown aniline staining mixtures, since the chemist tells us that it will dissolve or extract the other dyes. The compounding of iodinized and chromic acid media is regulated by fixed chemical principles.

Whether a general theory of staining can be founded upon purely chemical data, or purely biological, or partly biological and chemical data, is an unsolved problem. Dr. Beale (*Microscope in Medicine*, 4th edition, p. 61) claims that immediately after death the reaction of living matter is acid, and if an alkaline staining liquid be then applied the acid of the tissue will neutralize the alkaline stain, and we shall have a retention of color as a result. Ehrlich, Schwarze, and Westphal made a special study of stains, with a view to classify those used in microscopical technique, and found that certain tissues or cells had a special affinity for special dyes. And Hüppe (*Bakterien Forschung*, 1st edition, p. 31), commenting on their work, says: "This election, this preference of stains for certain elements, invests the staining process with the *value* of *chemical reactions*."

C. Saprophytic bacteria are divided into classes, ærobious and anærobious: the first requiring the presence of atmospheric gases in order to live, the second are enabled to round out their life-cycle only in an absence of these gases.

Investigations, then, have to be made to determine the effect of oxygen upon bacterial life, for the exclusion or the limitation of oxygen enables us to elucidate in part the decompositions of bacterial vegetation, and gives us a method of obtaining pure cultures of ærobious and anærobious varieties. (This method was explained by Fitz in the Proceedings of the German Chemical Society for 1884.)

There are two principal ways of ascertaining the effects of a deprivation of air.

I. *Exhaustion of the Air.*—(a) The atmospheric gases may be simply driven off by heat, either before or after the transplantation of the bacteria. Care must be taken not to destroy the bacteria in the use of heat. The apparatus employed is of a simple nature.

(b) We may adopt the plan of Nencki, which is more complicated than the preceding. The exit tube of Nencki's apparatus is opened, under an alkaline solution of pyrogallic acid, and a certain amount of the solution allowed to flow in when the exit tube is sealed. The alkaline solution of pyrogallic acid is a delicate reagent for detecting the presence of air in the apparatus. If the liquid assumes a blood-red hue, it indicates the presence of atmospheric air, and is an indication of an imperfectly performed experiment.

(c) In the methods described no provision is made for the escape of developed gases.

Pasteur (*Etudes Sur La Biere*) proposed a method in which a layer of oil, or of sterilized quicksilver, allowed the escape of gases, and prevented the absorption of air.

II. *Displacement of Air by Various Gases.*—In 1879 Gunning denied the efficiency of apparatus in which glass stopcocks, caoutchouc, quicksilver, or alkaline solution of pyrogallic acid were used, on the ground that they did not give absolute security. Gunning claimed that the most useful reagent for the detection of oxygen was the white ferrous ferrocyanide.

Fownes (Bridges' edition of *Fownes' Chemistry*, 1873, page 707) tells us, "With ferrous salts potassium ferrocyanide gives a precipitate which is perfectly white if air be excluded and the solution is quite free from ferric salts, but quickly turns blue on exposure to the air." Nencki and Lachowicz have proposed an elaborate apparatus in which hydrogen gas is made to displace the air, and the white ferrous ferrocyanide serves as a test for the complete absence of air. Dr. Hauser, in an article on the "Behavior of the Proteus Bacteria under Various Conditions of Life," describes a simple apparatus (made from two test-tubes) in which he experimented with hydrogen and carbon dioxide. Hauser says (*loc. cit.*, p. 51), "Auf diese Weise kann man Gelatin culturen in beliebige Gas arten dauernd einschliessen, und deren Wachstum bequem beobachten, ohne das ein entweichen des Gases denkbar wäre."

At a meeting of the British Association for 1885 a paper was presented by J. J. Coleman upon "The Action of Ozonized Air upon Microörganisms and Albumen in Solution." Coleman describes at length his experiment of passing air, artificially impregnated with ozone (by means of a Ruhmkorf coil), through a one per cent. solution of white of egg. He concludes that "albumen is practically indestructible by any atmospheric agency without previous splitting up by microörganisms."

The bearing of all these researches upon practical pathology can be readily seen to be of the greatest importance.

D. Chemistry, furthermore, aids bacteriology and hygiene in investigating the germicidal power of various agents. We must know how much carbolic acid, corrosive sublimate, iodoform, chlorine, and sulphur dioxide to use in order to completely destroy bacteria or their germs. Fisher and Proskauer have invented an apparatus for testing gaseous germicides. The results of the germicidal investigations of Koch and of Sternberg are daily put in practice by physicians and sanitarians.

E. Chemical changes in the tissues of the body

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may have something to do with the mycotic invasions, in many pathological processes, by preparing a suitable soil for their growth.

III. Having now reviewed some of the many ways in which bacteria are powerful from a chemical standpoint, and having taken some note of the aid given to bacteriology by the employment of chemical investigations, it remains to point out some practical bearings of phenomena alluded to in this paper. Bacteria do not thrive in acid media. This fact is daily made use of in the employment of vinegar as a preservative in many household operations. It has been proposed to apply this principle to the disinfection of sewage. Giglioli, an Italian authority, proposes (*Nature*, September 3d, 1885, p. 415) the use of acids. Since sewage is alkaline, and contains all the elements needed for the multiplication of bacteria, we can understand why microörganisms are rapidly developed therein; and Giglioli claims that the simplest and cheapest method for disinfecting sewage is to render its reaction permanently *acid*. Giglioli presents a strong argument for the use of acid when he claims that the great difficulty in extensive sewage disinfection has been to decide when the process is *complete*. In the employment of acids, disinfection, according to Giglioli, can be considered complete when the reaction is *permanently acid*.

The questions attending the chemical influence of bacteria become of practical importance to the agriculturist. Ensilage, a departure from the "stereotyped" mode of harvesting crops, has, at times, excited great interest. Mr. Fry, in a work on *Sweet Ensilage*, puts forward the view that bacterial fermentation is the cause of *souring* in the silo. Whenever the temperature in the silo is raised sufficiently high, by what Mr. Fry terms "intercellular oxidation," the bacteria present are destroyed and souring is prevented. The question is yet "sub judice," and further study is needed of the peculiar circumstances of the silo (*Nature*, October 22d, 1885, p. 607).

Under the stimulus given by the researches of Vaughn, the etiology, diagnosis, and treatment of summer diarrhœa in children are in a fair way to be soon placed on a firm scientific basis. A more careful examination of the urine and fæces in cases of diarrhœa in children is earnestly advocated. An attempt has been made to determine the relations between sulphovinic and oxy acids in the urine and putrid fermentation in the intestine. By means of chemical analysis we may, in the not distant future, be enabled to readily perceive in the urine of a child suffering from diarrhœa of septic origin indications which point to the cause of the disease. Special ptomaines, special bacteria, possibly, may be found in the examination of the fæces, which will give equally sure indications of the origin of the malady. Joining to this an examination of suspected food materials for tyrotoxicon or other ptomaines, and an antiseptic regimen, we may confidently hope to control the majority of cases of infantile septic diarrhœa. Henoch has given us a description of the symptoms which constitute "the clinical expression of the abnormal chemical process" in "intestinal dyspepsia," and has suggested the use of anti-fermentative remedies; and Holt, in a recent paper, has called the attention of the profession to the antiseptic treatment of the summer diarrhœa of children.

Fritsch has explained the action of bacteria in mycotic cystitis. They produce an alkaline decomposition of urine in the bladder. This infectious cystitis is often a grave disorder, but can be scientifically combated by antiseptic irrigation. (*The Diseases of Women*, Fritsch.)

The researches of Brieger, of Berlin, show that ptomaines resemble alkaloids of the higher plants in physiological action, and a suggestion has been made (H. G. Beyer) that, in order to establish an immunity from disease, we should employ alkaloids resembling the ptomaines in their action, or should administer physiological antagonists to the ptomaines. According to Hitchcock (*Am. Mo. Micr. Jour.*) the ptomaine produced by the bacterium of swine plague has been found (by Dr. Beyer) to resemble atropine in its action, and the same ptomaine has been successfully employed by Drs. Salmon and Smith to secure susceptible animals against attacks of swine plague.

In typhoid fever Dr. Jackson, of Virginia, has proposed the use of salts of ammonium to neutralize the waste of nitrogen. His theory is of interest since it is based upon a recognition of chemical changes produced in the body by microörganisms. He says: "This waste is undoubtedly owing to a waste of the nitrogenous constituents of the system caused by the life processes of a microzoon." Further on, in reference to the employment of ammonium nitrate as an antipyretic, Jackson says: "My own idea with regard to it is, that it is by inhibiting the life processes of the microbe by saturating it with the products of its own life, thus either crippling its vitality or altogether destroying its life on the principle of the law enunciated by me several years ago: no organism can exist in its own excretions, the product of its life processes" (Jackson: "Ammonia Treatment of Typhoid Fever," *Physician's Magazine*, August, 1885.

GUMMATOUS INFILTRATION OF THE TONGUE.—Four cases of the above lesion were reported by Dr. Urban G. Hitchcock at the last meeting of the American Laryngological Association.

In reviewing these cases, it is to be remarked that in no one of them was the fibrous septum of the tongue the exclusive seat of the deposit, which has been declared to select this tissue for its development, and that in three of the cases the deposit did not at all approach this structure. In no instance was there neighboring glandular enlargement. As might, perhaps, be anticipated, the degree of dysphagia produced by the growths was in direct proportion to the proximity of the deposit to the base of the tongue. Whether this is generally true does not appear from any works consulted. As far as these cases go they bear out the assumption which has been made to the effect that the soft palate and tongue are never simultaneously involved in ulceration.—*New York Medical Journal.*

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INSANITY AND THE CARE OF THE INSANE.

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(Read before the Medico-Legal Society of New York, March 9th, 1887.)

I. INSANITY.

INSANITY has been styled, and perhaps justly, *the* disease of civilization.

The greatest peril incurred, in the higher cultivation of the human intellect, is the danger of its derangement.

Stimulation or pressure upon the delicate organism of the brain oftentimes puts it out of order, and, like the intricate mechanism of the Geneva watch, one broken cog, or the presence and pressure of even a hair's weight, will derange its movement and impair its efficacy.

Man, in his original state, nearest to nature, the savage, the uncivilized, like the lower animals, knows little, if anything, of insanity. We may, therefore, with entire truth, say of insanity, that it is a fruit and product of what we call civilization.

Dr. Heber Newton calls it the scourge of the educated, the refined, the successful, the religious, the very nemesis of the nervous system.

Historically considered, it is but recently—within the lives of men now living—that insanity has been regarded, as it now seems to be generally recognized, as a state due to a diseased condition of the brain.

Science in this century has asserted, and substantially demonstrated, that the brain is the organ of what we call the mind, the seat and centre of thought, volition, will, and the intellectual faculties.

Shakespeare says: "Who shall minister to the mind diseased?" but modern science says that it is not the mind which is diseased, but the diseased *brain*, which reflects its distemper in the working and action of the mind.

Whether we examine earlier histories, traditions, ancient writers, or even the sacred writings, the madman, from the remotest periods, in all ages, among all nations and peoples, has been regarded, by the large majority of mankind prior to our century or era, as one afflicted of God, or possessed by an unclean spirit.

The New Testament scriptures seem to have warranted such a view, and the Church since Christ, especially throughout its earlier history, has inclined to this belief.

The influence of the moon, among the ancients, was so generally allied to madness that it gave the almost universal name of *lunatic* to the victim, and *lunacy* to the state or condition into which the foul fiend threw the sufferer.

The insane thus became objects of aversion, suspicion, and even abhorrence, to mankind, and there can be no doubt that all other sources of human misery and suffering are as a rush light to the sun when compared to what has been borne, endured, and suffered by the wretched insane throughout all the ages.

As science now regards insanity, this is the darkest record in human history against mankind; because, without excuse or palliation, it has shut out from even its sympathy these innocent victims of disease; has consigned them to living deaths more terrible than anything written in the *Inferno* of Dante, and stricken out of these suffering lives even the very word *hope*.

England has had its traditions, its superstitions, its shrines, its healing waters, its marvellous cures.

Scotland's healing wells are celebrated in verse.

Scott says, in *Marmion:*

> "Then to St. Fillian's blessed well,
> Whose spring can frenzied dreams dispel,
> And the crazed brain restore."

St. Ronan's Well was a place of great renown for the cure of lunatics, and our own poet, Whittier, has immortalized in verse the well of St. Maree, in Rossshire, situated on a small island of Loch-Maree:

> "And whoso bathes therein his brow
> With care or madness burning,
> Feels once again his healthful thought
> And sense of peace returning.
>
> "Oh! restless heart and fevered brain—
> Unquiet and unstable,
> That holy well of Loch-Maree
> Is more than idle fable."

The colony at Gheel, dating back more than 1000 years, owes its existence, and I may say its marvellous success, to the universal belief in the efficacy and curative powers of the shrine and church, which has been the Mecca toward which, for so many centuries, faith has led the pilgrim, children of the Church, to seek its curative powers at the shrine of St. Dymphna. The best authorities date the erection of this church in the twelfth century, but it is beyond question that a chapel, on the site of this church, preceded its erection for more than one century at the least.

At the tomb of the saint at Gheel, it is idle to deny, marvellous cures were wrought, and if, as Dr. Hack Tuke, in speaking of it, says, "it was the representative of the ecclesiastical treatment of mental diseases," it is well worthy the consideration of scientists and medical men to-day to inquire and determine how, and how far, the psychical and psychometrical effect of well-authenticated cases of marvellous cures could beneficially affect the disordered minds of the sixteenth, seventeenth, and eighteenth centuries who came to this shrine to be healed.

Dr. Hack Tuke, in his remarkable work, *History of the Insane in the British Islands*, gives at length many accounts of the superstitions and peculiar beliefs of the early Britons, concerning insanity, in England and Scotland, which would well repay perusal by those who desire to know the actual condition of the insane on those islands at the commencement of the present century, and the changes that have been wrought there in the condition, care, and treatment of the insane.

In speaking of insanity the first natural and pertinent inquiry is, what is insanity?

This is a question that most of the abler writers and alienists have attempted to answer.

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